

(FILE 'HOME' ENTERED AT 15:27:51 ON 08 JAN 2003)

FILE 'BIOSIS, CABA, CAPLUS, EMBASE, LIFESCI, MEDLINE, SCISEARCH,  
USPATFULL, JAPIO' ENTERED AT 15:28:24 ON 08 JAN 2003

L1	67824	S	ULCERATIVE COLITIS
L2	434	S	FUSOBACTERIUM VARIUM
L3	4413245	S	DIAGNOSIS
L4	2481696	S	DETECTION
L5	9	S	L1 AND L2
L6	2	S	L3 AND L5
L7	2	S	L4 AND L6
L8	602669	S	HIS
L9	3887	S	L1 AND L4
L10	1993	S	L9 AND L3
L11	1767	DUP REM	L10 (226 DUPLICATES REMOVED)
L12	1	S	L11 AND L2
L13	14471	S	L1 AND L3
L14	2	S	L13 AND L2
L15	3887	S	L1 AND L4
L16	3067	DUP REM	L15 (820 DUPLICATES REMOVED)
L17	12	S	L2 AND L3
L18	12	S	L2 AND L4
L19	1	DUP REM	L12 (0 DUPLICATES REMOVED)

(FILE 'HOME' ENTERED AT 15:27:51 ON 08 JAN 2003)

FILE 'BIOSIS, CABA, CAPLUS, EMBASE, LIFESCI, MEDLINE, SCISEARCH,  
USPATFULL, JAPIO' ENTERED AT 15:28:24 ON 08 JAN 2003

L1 67824 S ULCERATIVE COLITIS  
L2 434 S FUSOBACTERIUM VARIUM  
L3 4413245 S DIAGNOSIS  
L4 2481696 S DETECTION  
L5 9 S L1 AND L2  
L6 2 S L3 AND L5  
L7 2 S L4 AND L6  
L8 602669 S HIS  
L9 3887 S L1 AND L4  
L10 1993 S L9 AND L3  
L11 1767 DUP REM L10 (226 DUPLICATES REMOVED)  
L12 1 S L11 AND L2

L5 ANSWER 1 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 AB Background: Microbial agents are a possible cause of **ulcerative colitis**. We have previously reported evidence of bacteria invading the colonic mucosa of patients with **ulcerative colitis**. We have isolated bacteria from inflamed colonic mucosa, examined the localization of the species in the mucosa, and assayed for serum antibodies to the bacteria. Methods: Cohorts of 31 per group were enrolled from patients with active **ulcerative colitis**, Crohn's disease, ischemic colitis, and colon adenomas. A group of 31 healthy controls were also studied. The presence of bacteria in biopsies of patients with **ulcerative colitis** was analyzed by both isolation and immunohistochemistry. Sera from patients were tested for bacterial antibodies using both Western blots and enzyme-linked immunosorbent assay (ELISA). Results: Only sera from patients with **ulcerative colitis** gave specific reactions with **Fusobacterium varium** in Western blot assays. The detection rate of specific bands was higher for patients with **ulcerative colitis** (61%) than for subjects with either Crohn's disease (13%) or healthy controls (29%) ( $P < 0.001$  and  $P=0.021$ , respectively). The ELISA showed that the mean optical densities with extracts of *F. varium* as antigen were significantly higher for **ulcerative colitis** patients than for subjects with either Crohn's disease or healthy controls ( $P < 0.001$ ). Immunohistochemical detection of *F. varium* in colonic mucosa was significantly higher in patients with **ulcerative colitis** (84%) than for subjects with either Crohn's disease (16%) or other controls (3-13%) ( $P < 0.001$ ). Conclusions: **Fusobacterium varium** bacteria were present in a significant number of patients with active **ulcerative colitis**, and should be tested in therapeutic trials in order to confirm the causal relationship between *F. varium* and **ulcerative colitis**.

AN 2002:539792 BIOSIS  
 DN PREV200200539792  
 TI **Fusobacterium varium** localized in the colonic mucosa of patients with **ulcerative colitis** stimulates species-specific antibody.  
 AU Ohkusa, Toshifumi; Sato, Nobuhiro (1); Ogihara, Tatu; Morita, Koji; Ogawa, Masayuki; Okayasu, Isao  
 CS (1) Department of Gastroenterology, Juntendo University, School of Medicine, 2-1-1 Hongo, Bunkyo-ku, Tokyo, 113-8421: nsato@med.juntendo.ac.jp Japan  
 SO Journal of Gastroenterology and Hepatology, (August, 2002) Vol. 17, No. 8, pp. 849-853. <http://www.blackwell-science.com/jgh>. print. ISSN: 0815-9319.  
 DT Article  
 LA English

L5 ANSWER 2 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 AN 2002:519319 BIOSIS  
 DN PREV200200519319  
 TI **Fusobacterium varium** localized in the colonic mucosa of patients with **ulcerative colitis** stimulates species-specific antibody.  
 AU Ohkusa, Toshifumi (1); Sato, Nobuhiro; Miwa, Hiroto; Ogihara, Tatsuo; Terai, Takeshi; Kobayashi, Osamu; Morita, Koji; Ogawa, Masayuki; Okayasu, Isao  
 CS (1) Tokyo Japan  
 SO Gastroenterology, (April, 2002) Vol. 122, No. 4 Suppl. 1, pp. A-268. <http://www.gastrojournal.org/>. print. Meeting Info.: Digestive Disease Week and the 103rd Annual Meeting of the American Gastroenterological Association San Francisco, CA, USA May 19-22, 2002  
 ISSN: 0016-5085.  
 DT Conference

LA English

L5 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2003 ACS

AB Compns. for treatment of **ulcerative colitis** comprising a drug which can selectively kill **Fusobacterium varium** cells, or a drug which can neutralize the toxin produced by *F. varium* cells, a method for screening such a drug, a method for treating a patient with the disease, a vaccine for the disease, a diagnostic drug, a diagnostic method, an exptl. model for the disease and an exptl. animal for the disease are described. For example, the susceptibility of antimicrobial agents to *F. varium* was found to be in following order: tetracycline > penicillin > metronidazole > imipenem > amoxicillin, cefmetazole, ampicillin, fosfomycin, chloramphenicol. The bacteria was found to be resistant to clarithromycin, erythromycin, streptomycin, kanamycin and gentamycin.

AN 2002:946837 CAPLUS

DN 138:11422

TI Therapeutic agent for **ulcerative colitis**

IN Sato, Nobuhiro; Okusa, Toshifumi; Okayasu, Isao

PA Nobuhiro Sato, Japan

SO U.S. Pat. Appl. Publ., 4 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002187152	A1	20021212	US 2001-931951	20010820
	JP 2002363099	A2	20021218	JP 2001-172189	20010607
PRAI	JP 2001-172189	A	20010607		

L5 ANSWER 4 OF 9 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AB Background: Microbial agents are a possible cause of **ulcerative colitis**. We have previously reported evidence of bacteria invading the colonic mucosa of patients with **ulcerative colitis**. We have isolated bacteria from inflamed colonic mucosa, examined the localization of the species in the mucosa, and assayed for serum antibodies to the bacteria. Methods: Cohorts of 31 per group were enrolled from patients with active **ulcerative colitis**, Crohn's disease, ischemic colitis, and colon adenomas. A group of 31 healthy controls were also studied. The presence of bacteria in biopsies of patients with **ulcerative colitis** was analyzed by both isolation and immunohistochemistry. Sera from patients were tested for bacterial antibodies using both Western blots and enzyme-linked immunosorbent assay (ELISA). Results: Only sera from patients with **ulcerative colitis** gave specific reactions with **Fusobacterium varium** in Western blot assays. The detection rate of specific bands was higher for patients with **ulcerative colitis** (61%) than for subjects with either Crohn's disease (13%) or healthy controls (29%) ( $P < 0.001$  and  $P = 0.021$ , respectively). The ELISA showed that the mean optical densities with extracts of *F. varium* as antigen were significantly higher for **ulcerative colitis** patients than for subjects with either Crohn's disease or healthy controls ( $P < 0.001$ ). Immunohistochemical detection of *F. varium* in colonic mucosa was significantly higher in patients with **ulcerative colitis** (84%) than for subjects with either Crohn's disease (16%) or other controls (3-13%) ( $P < 0.001$ ). Conclusions: **Fusobacterium varium** bacteria were present in a significant number of patients with active **ulcerative colitis**, and should be tested in therapeutic trials in order to confirm the causal relationship between *F. varium* and **ulcerative colitis**. .COPYRGT. 2002 Blackwell Publishing Asia Pty Ltd.

AN 2002339906 EMBASE

TI **Fusobacterium varium** localized in the colonic mucosa  
 of patients with **ulcerative colitis** stimulates  
 species-specific antibody.  
 AU Ohkusa T.; Sato N.; Ogiwara T.; Morita K.; Ogawa M.; Okayasu I.  
 CS Dr. N. Sato, Department of Gastroenterology, Juntendo University, School  
 of Medicine, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan.  
 nsato@med.juntendo.ac.jp  
 SO Journal of Gastroenterology and Hepatology, (2002) 17/8 (849-853).  
 Refs: 27  
 ISSN: 0815-9319 CODEN: JGHEEO  
 CY Australia  
 DT Journal; Article  
 FS 004 Microbiology  
 005 General Pathology and Pathological Anatomy  
 026 Immunology, Serology and Transplantation  
 048 Gastroenterology  
 LA English  
 SL English  
  
 L5 ANSWER 5 OF 9 MEDLINE  
 AB BACKGROUND: Bacteria are implicated in certain forms of model chronic  
 colitis but the identity and role of bacteria in human **ulcerative  
 colitis** (UC) are uncertain. AIMS: To isolate pathogenic bacteria  
 from inflamed mucosa of patients with UC, to examine whether the bacteria  
 have a toxin to Vero cells, and to determine whether the toxin induces  
 UC-like lesions in animals. METHODS: Bacteria were isolated from UC  
 patients and supernatants from cultures were filtered and tested for  
 cytotoxicity to Vero cells. Bacterial cells producing the cytotoxic  
 supernatants were examined by polymerase chain reaction for verotoxin  
 genes. Culture supernatants of cytotoxic strains were examined by high  
 performance liquid chromatography for organic acid concentrations. Mice  
 were given enemas containing organic acid at the mean concentration in the  
 supernatants of cytotoxic strains to ascertain whether colonic lesions  
 appear in UC. RESULTS: Only supernatants from cultures of  
**Fusobacterium varium** killed Vero cells. Bacterial cells  
 lacked verotoxin genes. Bacterial culture supernatants contained high  
 concentrations of n-butyric acid and the mean concentration (32 mmol/l)  
 was cytotoxic to Vero cells. Twenty four hours after mice were given  
 enemas containing either butyric acid or F varium culture supernatants,  
 colonic ulcers with crypt abscesses, inflammatory cell infiltration, and  
 apoptotic changes were observed. CONCLUSIONS: Butyric acid in culture  
 supernatants from cultures of F varium caused UC-like lesions in mice.  
 This study indicates that F varium may be one of the elusive pathogenic  
 factors in UC.  
 AN 2003004469 IN-PROCESS  
 DN 22365798 PubMed ID: 12477765  
 TI Induction of experimental **ulcerative colitis** by  
**Fusobacterium varium** isolated from colonic mucosa of  
 patients with **ulcerative colitis**.  
 AU Ohkusa T; Okayasu I; Ogiwara T; Morita K; Ogawa M; Sato N  
 CS Department of Gastroenterology, Juntendo University, School of Medicine,  
 Tokyo, Japan.  
 SO GUT, (2003 Jan) 52 (1) 79-83.  
 Journal code: 2985108R. ISSN: 0017-5749.  
 CY England: United Kingdom  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS IN-PROCESS; NONINDEXED; Abridged Index Medicus Journals; Priority Journals  
 ED Entered STN: 20030105  
 Last Updated on STN: 20030105  
  
 L5 ANSWER 6 OF 9 MEDLINE  
 AB BACKGROUND: Microbial agents are a possible cause of **ulcerative  
 colitis**. We have previously reported evidence of bacteria invading

the colonic mucosa of patients with **ulcerative colitis**. We have isolated bacteria from inflamed colonic mucosa, examined the localization of the species in the mucosa, and assayed for serum antibodies to the bacteria. METHODS: Cohorts of 31 per group were enrolled from patients with active **ulcerative colitis**, Crohn's disease, ischemic colitis, and colon adenomas. A group of 31 healthy controls were also studied. The presence of bacteria in biopsies of patients with **ulcerative colitis** was analyzed by both isolation and immunohistochemistry. Sera from patients were tested for bacterial antibodies using both Western blots and enzyme-linked immunosorbent assay (ELISA). RESULTS: Only sera from patients with **ulcerative colitis** gave specific reactions with **Fusobacterium varium** in Western blot assays. The detection rate of specific bands was higher for patients with **ulcerative colitis** (61%) than for subjects with either Crohn's disease (13%) or healthy controls (29%) ( $P < 0.001$  and  $P = 0.021$ , respectively). The ELISA showed that the mean optical densities with extracts of *F. varium* as antigen were significantly higher for **ulcerative colitis** patients than for subjects with either Crohn's disease or healthy controls ( $P < 0.001$ ). Immunohistochemical detection of *F. varium* in colonic mucosa was significantly higher in patients with **ulcerative colitis** (84%) than for subjects with either Crohn's disease (16%) or other controls (3-13%) ( $P < 0.001$ ). CONCLUSIONS: **Fusobacterium varium** bacteria were present in a significant number of patients with active **ulcerative colitis**, and should be tested in therapeutic trials in order to confirm the causal relationship between *F. varium* and **ulcerative colitis**.

AN 2002410989 MEDLINE  
 DN 22155263 PubMed ID: 12164960  
 TI **Fusobacterium varium** localized in the colonic mucosa of patients with **ulcerative colitis** stimulates species-specific antibody.  
 AU Ohkusa Toshifumi; Sato Nobuhiro; Ogiwara Tatuio; Morita Koji; Ogawa Masayuki; Okayasu Isao  
 CS Department of Gastroenterology, Juntendo University, School of Medicine, Tokyo, Japan.  
 SO JOURNAL OF GASTROENTEROLOGY AND HEPATOLOGY, (2002 Aug) 17 (8) 849-53. Journal code: 8607909. ISSN: 0815-9319.  
 CY Australia  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 200211  
 ED Entered STN: 20020808  
 Last Updated on STN: 20021212  
 Entered Medline: 20021119

L5 ANSWER 7 OF 9 SCISEARCH COPYRIGHT 2003 ISI (R)

AB Background: Microbial agents are a possible cause of **ulcerative colitis**. We have previously reported evidence of bacteria invading the colonic mucosa of patients with **ulcerative colitis**. We have isolated bacteria from inflamed colonic mucosa, examined the localization of the species in the mucosa, and assayed for serum antibodies to the bacteria.  
 Methods: Cohorts of 31 per group were enrolled from patients with active **ulcerative colitis**, Crohn's disease, ischemic colitis, and colon adenomas. A group of 31 healthy controls were also studied. The presence of bacteria in biopsies of patients with **ulcerative colitis** was analyzed by both isolation and immunohistochemistry. Sera from patients were tested for bacterial antibodies using both Western blots and enzyme-linked immunosorbent assay (ELISA).  
 Results: Only sera from patients with **ulcerative**

colitis gave specific reactions with **Fusobacterium varium** in Western blot assays. The detection rate of specific bands was higher for patients with **ulcerative colitis** (61%) than for subjects with either Crohn's disease (13%) or healthy controls (29%) ( $P < 0.001$  and  $P = 0.021$ , respectively). The ELISA showed that the mean optical densities with extracts of *F. varium* as antigen were significantly higher for **ulcerative colitis** patients than for subjects with either Crohn's disease or healthy controls ( $P < 0.001$ ). Immunohistochemical detection of *F. varium* in colonic mucosa was significantly higher in patients with **ulcerative colitis** (84%) than for subjects with either Crohn's disease (16%) or other controls (3-13%) ( $P < 0.001$ ).

Conclusions: **Fusobacterium varium** bacteria were present in a significant number of patients with active **ulcerative colitis**, and should be tested in therapeutic trials in order to confirm the causal relationship between *F. varium* and **ulcerative colitis**. (C) 2002 Blackwell Publishing Asia Pty Ltd.

AN 2002:672177 SCISEARCH

GA The Genuine Article (R) Number: 581GB

TI **Fusobacterium varium** localized in the colonic mucosa of patients with **ulcerative colitis** stimulates species-specific antibody

AU Ohkusa T; Sato N (Reprint); Ogihara T; Morita K; Ogawa M; Okayasu I

CS Juntendo Univ, Sch Med, Dept Gastroenterol, Bunkyo Ku, 2-1-1 Hongo, Tokyo 1138421, Japan (Reprint); Juntendo Univ, Sch Med, Dept Gastroenterol, Bunkyo Ku, Tokyo 1138421, Japan; Kyorin Univ, Sch Hlth Sci, Dept Microbiol, Hachioji, Tokyo, Japan; Kawasaki City Inst Publ Hlth, Kawasaki, Kanagawa, Japan; Kitasato Univ, Sch Med, Dept Pathol, Sagamihara, Kanagawa 228, Japan

CYA Japan

SO JOURNAL OF GASTROENTEROLOGY AND HEPATOLOGY, (AUG 2002) Vol. 17, No. 8, pp. 849-853.

Publisher: BLACKWELL PUBLISHING ASIA, 54 UNIVERSITY ST, P O BOX 378, CARLTON, VICTORIA 3053, AUSTRALIA.

ISSN: 0815-9319.

DT Article; Journal

LA English

REC Reference Count: 27

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

L5 ANSWER 8 OF 9 SCISEARCH COPYRIGHT 2003 ISI (R)

AN 2002:416207 SCISEARCH

GA The Genuine Article (R) Number: 548AW

TI **Fusobacterium varium** localized in the colonic mucosa of patients with **ulcerative colitis** stimulates species-specific antibody

AU Ohkusa T (Reprint); Sato N; Miwa H; Ogihara T; Terai T; Kobayashi O; Morita K; Ogawa M; Okayasu I

SO GASTROENTEROLOGY, (APR 2002) Vol. 122, No. 4, Supp. [1], pp. A268-A268. MA M1092.

Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399 USA.

ISSN: 0016-5085.

DT Conference; Journal

LA English

REC Reference Count: 0

L5 ANSWER 9 OF 9 USPATFULL

AB Disclosed are pharmaceutical compositions of treatment for a patient with **ulcerative colitis** comprising a drug which can selectively kill **Fusobacterium varium** cells, or a drug which can neutralize the toxin produced by **Fusobacterium varium** cells, a method for screening such a drug, a method for treating a patient with the disease, a vaccine for the disease, a

diagnostic drug, a diagnostic method, an experimental model for the  
disease and an experimental animal for the disease.

AN 2002:329473 USPATFULL

TI Therapeutic agent for **ulcerative colitis**

IN Sato, Nobuhiro, Tokyo, JAPAN  
Okusa, Toshifumi, Tokyo, JAPAN  
Okayasu, Isao, Sagamihara-Shi, JAPAN

PA Nobuhiro SATO, Suginami-Ku, JAPAN (non-U.S. corporation)

PI US 2002187152 A1 20021212

AI US 2001-931951 A1 20010820 (9)

PRAI JP 2001-172189 20010607

DT Utility

FS APPLICATION

LREP OBLON SPIVAK MCCLELLAND MAIER & NEUSTADT PC, FOURTH FLOOR, 1755  
JEFFERSON DAVIS HIGHWAY, ARLINGTON, VA, 22202

CLMN Number of Claims: 15

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 318

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=>